WO 03/106498

SEQUENCE LISTING

<110> Crucell Holland B.V. Bakker, Alexander B.H. Meester-Rood, Pauline M.L. Bakker, Adrianus Q. <120> AGONISTIC BINDING MOLECULES TO THE HUMAN OX40 RECEPTOR <130> 0077 WO 00 ORD <150> PCT/NL02/00389 <151> 2002-06-13 <160> 54 <170> PatentIn version 3.1 <210> 1 <211> 769 <212> DNA <213> Artificial sequence <220> <223> scFv SC02008 <220> <221> CDS <222> (3)..(767) <223> <400> 1 cc atg gct gag gtg cag ctg gtg gag tct ggg gga ggc ttg gtc cag Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln 47 10 cct gga ggg tcc ctg aga ctc tcc tgt gca gcc tct gga ttc acc ttt Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe 95

25

20

÷,

agc Ser	aac Asn	tac Tyr	acg Thr 35	atg Met	aac Asn	tgg Trp	gtc Val	cgc Arg 40	cag Gln	gcg Ala	ccc Pro	GJ À aaa	aag Lys 45	GJ À âââ	ctg Leu	143
gag Glu	tgg Trp	gtc Val 50	tca Ser	gct Ala	att Ile	agt Ser	ggt Gly 55	agt Ser	ggt Gly	ggt Gly	agc Ser	aca Thr 60	tac Tyr	tac Tyr	gca Ala	191
gac Asp	tcc Ser 65	gtg Val	aag Lys	ggc Gly	cgg Arg	ttc Phe 70	acc Thr	atc Ile	tcc Ser	aga Arg	gac Asp 75	aat Asn	tcc Ser	aag Lys	aac Asn	239
acg Thr 80	ctg Leu	tat Tyr	ctg Leu	caa Gln	atg Met 85	aac Asn	agc Ser	ctg Leu	aga Arg	gcc Ala 90	gag Glu	gac Asp	acg Thr	gcc Ala	gtg Val 95	287
tat Tyr	tac Tyr	tgt Cys	gcc Ala	aaa Lys 100	gac Asp	cgc Arg	tac Tyr	tcc Ser	cag Gln 105	gtg Val	cac His	tac Tyr	gcg Ala	ttg Leu 110	gat Asp	335
tac Tyr	tgg Trp	ggc Gly	cag Gln 115	ggc Gly	acc Thr	ctg Leu	gtg Val	acc Thr 120	gtg Val	ctc Leu	gag Glu	ggt Gly	acc Thr 125	gga Gly	ggt Gly	383
tcc Ser	ggc Gly	gga Gly 130	acc Thr	Gly	tct Ser	GJÀ āāā	act Thr 135	ggt Gly	acg Thr	agc Ser	gag Glu	ctc Leu 140	gac Asp	atc Ile	cag Gln	431
atg Met	acg Thr 145	cag Gln	tct Ser	cca Pro	gac Asp	tca Ser 150	ctg Leu	ccc Pro	gtc Val	acc Thr	cct Pro 155	gga Gly	gag Glu	ccg Pro	gcc Ala	479
tcc Ser 160	atc Ile	tcc Ser	tgc Cys	agg Arg	tct Ser 165	agt Ser	cag Gln	agc Ser	ctc Leu	ctg Leu 170	cat His	agt Ser	aat Asn	gga Gly	tac Tyr 175	527
aac Asn	tat Tyr	ttg Leu	gat Asp	tgg Trp 180	tac Tyr	ctg Leu	cag Gln	aag Lys	gca Ala 185	GJ À aaa	cag Gln	tct Ser	cca Pro	cag Gln 190	ctc Leu	575
ctg Leu	atc Ile	tat Tyr	ttg Leu 195	ggt Gly	tct Ser	aat Asn	cgg Arg	gcc Ala 200	tcc Ser	GJA aaa	gtc Val	cct Pro	gac Asp 205	agg Arg	ttc Phe	623
agt Ser	ggc Gly	agt Ser 210	gga Gly	tca Ser	ggc Gly	aca Thr	gat Asp 215	ttt Phe	aca Thr	ctg Leu	aaa Lys	atc Ile 220	agc Ser	aga Arg	gtg Val	671
gag Glu	gct Ala 225	gag Glu	gat Asp	gtt Val	GJÀ aaa	gtt Val 230	tat Tyr	tac Tyr	tgc Cys	cag Gln	cag Gln 235	tac Tyr	tac Tyr	aac Asn	cac His	719
ccg Pro 240	acg Thr	acc Thr	ttc Phe	ggc Gly	cag Gln 245	ggc Gly	acc Thr	aaa Lys	ctg Leu	gaa Glu 250	atc Ile	aaa Lys	cgc Arg	gcg Ala	gcc Ala 255	767
gc																769

<210> 2

<211> 255

<212> PRT

<213> Artificial sequence

<220>

<223> scFv SC02008

<400> 2

Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro 1 5 10 15

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser 20 25 30

Asn Tyr Thr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu 35 40

Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr 85 90 95

Tyr Cys Ala Lys Asp Arg Tyr Ser Gln Val His Tyr Ala Leu Asp Tyr 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser 115 120 125

Gly Gly Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile Gln Met 130 140

Thr Gln Ser Pro Asp Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser 145 150 155 160

Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn 165 170 175

Tyr Leu Asp Trp Tyr Leu Gln Lys Ala Gly Gln Ser Pro Gln Leu Leu 180 185 190

Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser 195 200 205

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu 210 215 220

Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr Tyr Asn His Pro 225 230 235 240

Thr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Ala Ala 245 250 255

<210> 3 <211> 775 <212> DNA <213> Artificial sequence <220> <223> scFv SC02009 <220> <221> CDS <222> (3)..(773)<223> <400> 3 cc atg gct gag gtg cag ctg gtg gag tct ggg gga ggc ttg gtc cag 47 Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln 5 cct ggg ggg tcc ctg aga ctc tcc tgt gca gcc tct gga ttc acc ttc 95 Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe 20 25 age gge tae tet atg aac tgg gte ege cag geg eee ggg aag ggg etg 143 Ser Gly Tyr Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu gag tgg gtt ggc cgt act aga aac aaa gct aac agt tac acc aca gaa 191 Glu Trp Val Gly Arg Thr Arg Asn Lys Ala Asn Ser Tyr Thr Thr Glu 55 tac gcc gcg tct gtg aaa ggc aga ttc acc atc tca aga gat gat tca 239 Tyr Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser aag aac tca ctg tat ctg caa atg aac agt ctg aga gcc gag gac aca 287 Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr 85 90 gcc gtg tat tac tgt gcc aaa gac cgc tac gtc aac acg tcg aac gcg Ala Val Tyr Tyr Cys Ala Lys Asp Arg Tyr Val Asn Thr Ser Asn Ala 100 ttc gat tac tgg ggc cag ggc acc ctg gtg acc gtg ctc gag ggt acc 383 Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr gga ggt tee gge gga ace ggg tet ggg act ggt acg age gag ete gae 431 Gly Gly Ser Gly Gly Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp atc cag atg aca cag tot cca gac toa ctg ccc gtc acc cct gga gag 479 Ile Gln Met Thr Gln Ser Pro Asp Ser Leu Pro Val Thr Pro Gly Glu 150 155

ccg gcc Pro Ala 160	tcc atc Ser Ile	tcc tg Ser Cy 16	s Arg	tct Ser	agt Ser	cag Gln	agc Ser 170	ctc Leu	ctg Leu	cat His	agt Ser	aat Asn 175	52	27
gga tac Gly Tyr	aac tat Asn Tyr	ttg ga Leu As 180	t tgg p Trp	tac Tyr	ctg Leu	cag Gln 185	aag Lys	cca Pro	Gly	cag Gln	tct Ser 190	cca Pro	57	75
cag ctc Gln Leu	ctg atc Leu Ile 195	tat tt Tyr Le	g ggt u Gly	tct Ser	aat Asn 200	cgg Arg	gcc Ala	tcc Ser	G] À âââ	gtc Val 205	cct Pro	gac Asp	62	23
agg ttc Arg Phe	agt ggc Ser Gly 210	agt gg Ser Gl	a tca y Ser	ggc Gly 215	aca Thr	gat Asp	ttt Phe	aca Thr	ctg Leu 220	aaa Lys	atc Ile	agc Ser	67	71
aga gtg Arg Val 225	gag gct Glu Ala	cac ca His Hi	t gtt s Val 230	GJ y ggg	gtt Val	tat Tyr	tac Tyr	tgc Cys 235	cag Gln	cag Gln	tac Tyr	ccg Pro	71	19
ctg ggc Leu Gly 240	ccg ccc Pro Pro	acc tt Thr Ph 24	e Gly	cag Gln	ggc Gly	acc Thr	aaa Lys 250	ctg Leu	gaa Glu	atc Ile	aaa Lys	cgc Arg 255	76	57
gcg gcc Ala Ala	gc												77	75
<210> 4														
<211> 2	57													
<212> P	RT													
<213> A	rtificia	al sequ	ence											
<220>														
<223> s	cFv SC0	2009												
<400> 4														
Met Ala 1	Glu Val	Gln Le	ı Val	Glu	Ser	Gly 10	Gly	Gly	Leu	Val	Gln 15	Pro		
Gly Gly	Ser Leu 20	Arg Le	ı Ser	Суз	Ala 25	Ala	Ser	Gly	Phe	Thr 30	Phe	Ser		
Gly Tyr	Ser Met 35	Asn Tr	Val	Arg 40	Gln	Ala	Pro	Gly	Lys 45	Gly	Leu	Glu		
Trp Val	Gly Arg	Thr Ar	J Asn 55	Lys	Ala	Asn	Ser	Tyr 60	Thr	Thr	Glu	туг		
Ala Ala 65	Ser Val	Lys Gl	/ Arg	Phe	Thr	Ile	Ser 75	Arg	Asp	Asp	Ser	Lys 80		

5/46

Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala 85 90 95

Val Tyr Tyr Cys Ala Lys Asp Arg Tyr Val Asn Thr Ser Asn Ala Phe 100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly 115 120 125

Gly Ser Gly Gly Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile 130 135 140

Gln Met Thr Gln Ser Pro Asp Ser Leu Pro Val Thr Pro Gly Glu Pro 145 150 155 160

Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly
165 170 175

Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln 180 185 190

Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg 195 200 205

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg 210 215 220

Val Glu Ala His His Val Gly Val Tyr Tyr Cys Gln Gln Tyr Pro Leu 225 230 235 240

Gly Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Ala 245 250 255

Ala

<210> 5

<211> 736

<212> DNA

<213> Artificial sequence

<220>

<223> scFv SC02010

<220>

<221> CDS

<222> (3)..(734)

<223>

<400> 5 cc atg gct Met Ala 1	gag gtg Glu Val	cag ctg gt Gln Leu Va 5	al Glu Ser (ggg gga ggc t Gly Gly I 10	etg atc cag Seu Ile Gln 15	47
cct ggg gg Pro Gly Gl	g tcc ctg y Ser Leu 20	aga ctc t Arg Leu S	tcc tgt gca Ser Cys Ala 25	gcc tct gga Ala Ser Gly	ttc acc ttc Phe Thr Phe 30	95
agc ggc ta Ser Gly Ty	c cct atg r Pro Met 35	aac tgg g Asn Trp V	gtc cgc cag Val Arg Gln 40	gcg ccc ggg Ala Pro Gly	aag ggg cto Lys Gly Lew 45	143
gag tgg gt Glu Trp Va 50	g gca gtt l Ala Val	Ile Ser T	tat gat gga Tyr Asp Gly 55	agt aat aaa Ser Asn Lys 60	tac tac gca Tyr Tyr Ala	191 1
gac tcc gt Asp Ser Va 65	g aag ggc l Lys Gly	cga ttc a Arg Phe T 70	acc atc tcc Thr Ile Ser	aga gac aat Arg Asp Asn 75	tcc aag aac Ser Lys Asr	239 1
acg ctg ta Thr Leu Ty 80	t ctg caa r Leu Gln	atg aac a Met Asn S 85	agc ctg aga Ser Leu Arg	gct gag gac Ala Glu Asp 90	aca gcc gtc Thr Ala Val 95	g 287 L
tat tac to Tyr Tyr Cy	t gca aga s Ala Arg 100	Asp Met S	tcc ggc ttc Ser Gly Phe 105	cac gag ttc His Glu Phe	gat tac tgg Asp Tyr Trp 110	335
ggc cag gg Gly Gln Gl	c acc ctg y Thr Leu 115	gtg acc g Val Thr V	gtg ctc gag Val Leu Glu 120	ggt acc gga Gly Thr Gly	ggt tcc ggd Gly Ser Gly 125	383
gga acc gg Gly Thr Gl 13	y Ser Gly	Thr Gly T	acg agc gag Thr Ser Glu 135	ctc acc cag Leu Thr Gln 140	tct cca tcc Ser Pro Ser	431
tcc ctg tc Ser Leu Se 145	t gca tct r Ala Ser	gta gga g Val Gly A 150	gac aga gtc Asp Arg Val	acc atc act Thr Ile Thr 155	tgc cgg gca Cys Arg Ala	a 479 a
				tat cag cag Tyr Gln Gln 170		7
		Leu Ile T		tcc agt ttg Ser Ser Leu		
gtc cca to Val Pro Se	a agg tto r Arg Phe 195	agt ggc a Ser Gly S	agt gga tct Ser Gly Ser 200	ggg aca gat Gly Thr Asp	ttc act ctc Phe Thr Let 205	623
acc atc ag Thr Ile Se 21	r Ser Leu	Gln Pro G	gaa gat ttt Glu Asp Phe 215	gca act tac Ala Thr Tyr 220	tac tgt caa Tyr Cys Glr	a 671 1
cag agt ta Gln Ser Ty 225	c agt acc r Ser Thr	cct cca a Pro Pro T 230	acg ttc ggc Thr Phe Gly	caa ggg acc Gln Gly Thr 235	aag gtg gag Lys Val Glu	719 1
atc aaa co Ile Lys Ar 240						736

<210> 6

<211> 244

<212> PRT

<213> Artificial sequence

<220>

<223> scFv SC02010

<400> 6

Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Leu Ile Gln Pro 1 5 10 15

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser 20 25 30

Gly Tyr Pro Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu 35 40 45

Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp 50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Ala Arg Asp Met Ser Gly Phe His Glu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser Gly Gly 115 120 125

Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Thr Gln Ser Pro Ser Ser 130 135 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser 145 150 155 160

Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys 165 170 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr 195 200 205

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln 210 215 220

Ser Tyr Ser Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile 225 230 235 240

Lys Arg Ala Ala

<210> 7

<211> 763

<212> DNA

<213> Artificial sequence

<220>

<223> scFv SC02011

<220>

<221> CDS

<222> (3)..(761)

<223>

<400> 7 cc atg gct gag gtg cag ctg gtg gag tct ggg gga ggc gtg gtc cag 47 Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Val Val Gln 10 cct ggg agg tcc ctg aga ctc tcc tgt gca gcc tct gga ttc acc ttc 95 Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe 20 25 agc gac tac acg atg aac tgg gtc cgc cag gcg ccc ggg aag ggg ctg 143 Ser Asp Tyr Thr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu gag tgg gtc tca tcc att agt ggt ggt agc aca tac tac gca gac tcc 191 Glu Trp Val Ser Ser Ile Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser 55 agg aag ggc aga ttc acc atc tcc aga gac aat tcc aag aac acg ctg 239 Arg Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu 70 tat ctt caa atg aac aac ctg aga gct gag gac acg gcc gtg tat tac 287 Tyr Leu Gln Met Asn Asn Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr 85 tgt gca aga gac cgc tac ttc agg cag cag aac gcg ttc gat tac tgg 335 Cys Ala Arg Asp Arg Tyr Phe Arg Gln Gln Asn Ala Phe Asp Tyr Trp 105 ggc cag ggc acc ctg gtg acc gtg ctc gag ggt acc gga ggt tcc ggc 383

Gly Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser Gly

gga a Gly T	cc ggg hr Gly 130	Ser	Gly	act Thr	ggt Gly	acg Thr 135	agc Ser	gag Glu	ctc Leu	gac Asp	atc Ile 140	cag Gln	atg Met	act Thr	431
Gln S	ct cca er Pro 45	gtc Val	acc Thr	ctg Leu	ccc Pro 150	gtc Val	acc Thr	cct Pro	gga Gly	gag Glu 155	ccg Pro	gcc Ala	tcc Ser	atc Ile	479
tcc to Ser Co 160	gc agg ys Arg	tct Ser	agt Ser	cag Gln 165	agc Ser	ctc Leu	ctg Leu	cat His	agt Ser 170	aat Asn	gga Gly	tac Tyr	aac Asn	tat Tyr 175	527
ttg ga Leu A	at tgg sp Trp	tac Tyr	ctg Leu 180	cag Gln	aag Lys	cca Pro	Gly ggg	cag Gln 185	tct Ser	cca Pro	cag Gln	ctc Leu	ctg Leu 190	atc Ile	575
tat ti Tyr Le	tg ggt eu Gly	tct Ser 195	aat Asn	cgg Arg	gcc Ala	tcc Ser	999 999 200	gtc Val	cct Pro	gac Asp	agg Arg	ttc Phe 205	agt Ser	ggc Gly	623
agt go Ser G	ga tca ly Ser 210	ggc Gly	aca Thr	gat Asp	ttt Phe	aca Thr 215	ctg Leu	aaa Lys	atc Ile	agc Ser	aga Arg 220	gtg Val	gag Glu	gct Ala	671
Glu As	at gtt sp Val 25	GJÅ āāā	gtt Val	tat Tyr	tac Tyr 230	tgc Cys	cag Gln	cag Gln	tac Tyr	ctc Leu 235	acg Thr	gcc Ala	ccg Pro	ccc Pro	719
acc ti Thr Pl 240	tc ggc he Gly	cag Gln	ggc Gly	acc Thr 245	aaa Lys	ctg Leu	gaa Glu	atc Ile	aaa Lys 250	cgc Arg	gcg Ala	gcc Ala	gc		763
<210>	8														
<211>	253														
<212>	PRT														
<213>	Arti	ficia	al se	equer	ıce										
<220>															
<223>	scFv	SC02	2011												
<400>	8														
Met Al	la Glu	Val	Gln 5	Leu	Val	Glu	Ser	Gly 10	Gly	Gly	Val	Val	Gln 15	Pro	
Gly A	rg Ser	Leu 20	Arg	Leu	Ser	Cys	Ala 25	Ala	Ser	Gly	Phe	Thr 30	Phe	Ser	
Asp Ty	yr Thr 35	Met	Asn	Trp	Val	Arg 40	Gln	Ala	Pro	Gly	Lys 45	Gly	Leu	Glu	

Trp Val Ser Ser Ile Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Arg 50 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 65 70 75 80

Leu Gln Met Asn Asn Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Tyr Phe Arg Gln Gln Asn Ala Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser Gly Gly 115 120 125

Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile Gln Met Thr Gln 130 135 140

Ser Pro Val Thr Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser 145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu 165 170 175

Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr 180 185 190

Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu 210 215 220

Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr Leu Thr Ala Pro Pro Thr 225 230 235 240

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Ala Ala 245 250

<210> 9

<211> 748

<212> DNA

<213> Artificial sequence

<220>

<223> scFv SC02012

<220>

<221> CDS

<222> (3)..(746)

<223>

ı	atg q	9 gct (Ala (gaa (Glu '	Val (cag (Gln) 5	ctg (Leu '	gtg (Val (gaa a Slu s	Ser (ggc (Gly (ggc (ggc (Gly)	ctg (Leu)	Val 1	aag Lys 15	47
ccg Pro	ggt Gly	ggc Gly	agc Ser	ctg Leu 20	cgc Arg	ctg Leu	agc Ser	tgc Cys	gcc Ala 25	gct Ala	agc Ser	ggc Gly	ttc Phe	acc Thr 30	ttt Phe	95
agc Ser	aac Asn	gac Asp	tcg Ser 35	atg Met	aac Asn	tgg Trp	atg Met	cgc Arg 40	cag Gln	gcc Ala	ccg Pro	ggc	aaa Lys 45	ggc Gly	ctc Leu	143
gaa Glu	tgg Trp	gtg Val 50	gcc Ala	aat Asn	atc Ile	aat Asn	cag Gln 55	gat Asp	ggc Gly	aac Asn	gaa Glu	aaa Lys 60	tat Tyr	tac Tyr	gcc Ala	191
gac Asp	tct Ser 65	gtc Val	aaa Lys	ggc Gly	cgc Arg	ttc Phe 70	acc Thr	atc Ile	agt Ser	cgc Arg	gat Asp 75	aac Asn	tcc Ser	aaa Lys	aac Asn	239
tcc Ser 80	ctg Leu	tac Tyr	ctg Leu	cag Gln	atg Met 85	aac Asn	agc Ser	ctg Leu	cgc Arg	gac Asp 90	gaa Glu	gat Asp	acc Thr	gcc Ala	ctg Leu 95	287
tac Tyr	tac Tyr	tgc Cys	gca Ala	cgc Arg 100	gcc Ala	cgc Arg	gcc Ala	gcc Ala	ggc Gly 105	acc Thr	atc Ile	ttc Phe	gat Asp	tac Tyr 110	tgg Trp	335
ggc Gly	cag Gln	ggc Gly	acc Thr 115	ctg Leu	gtg Val	acc Thr	gtg Val	ctc Leu 120	gag Glu	ggt Gly	acc Thr	gga Gly	ggt Gly 125	tcc Ser	ggc Gly	383
gga Gly	acc Thr	ggg Gly 130	tct Ser	GJÀ aaa	act Thr	ggt Gly	acg Thr 135	agc Ser	gag Glu	ctc Leu	gat Asp	atc Ile 140	cag Gln	atg Met	acc Thr	431
cag Gln	agc Ser 145	ccg Pro	agt Ser	tcc Ser	ctg Leu	agc Ser 150	gcc Ala	tcc Ser	gtg Val	ggc Gly	gac Asp 155	cgc Arg	gtg Val	acc Thr	atc Ile	479
acc Thr 160	tgc Cys	cgc Arg	gcc Ala	agc Ser	cag Gln 165	aac Asn	gtc Val	agc Ser	aac Asn	tac Tyr 170	ctg Leu	acc Thr	tgg Trp	tac Tyr	cag Gln 175	527
					gct Ala											575
ctc Leu	caa Gln	agc Ser	ggc Gly 195	gtg Val	ccg Pro	tct Ser	aga Arg	ttc Phe 200	agt Ser	ggc Gly	tcc Ser	ggc Gly	tcc Ser 205	gga Gly	acc Thr	623
gat Asp	ttt Phe	acc Thr 210	ctg Leu	acc Thr	atc Ile	agc Ser	agc Ser 215	ctg Leu	cag Gln	ccg Pro	gaa Glu	gat Asp 220	ttc Phe	gct Ala	acc Thr	671
tac Tyr	tat Tyr 225	tgt Cys	cag Gln	cag Gln	tcc Ser	tac Tyr 230	ttc Phe	aac Asn	ccg Pro	gcg Ala	acc Thr 235	ttc Phe	ggc Gly	cag Gln	ggc ggc	719
acc Thr 240	aaa Lys	ctg Leu	gaa Glu	atc Ile	aaa Lys 245	cgc Arg	gcg Ala	gcc Ala	gc							748

<210> 10

<211> 248

<212> PRT

<213> Artificial sequence

<220>

<223> scFv SC02012

<400> 10

Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro 1 5 10 15

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser 20 25 30

Asn Asp Ser Met Asn Trp Met Arg Gln Ala Pro Gly Lys Gly Leu Glu 35 40 45

Trp Val Ala Asn Ile Asn Gln Asp Gly Asn Glu Lys Tyr Tyr Ala Asp 50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser 65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Leu Tyr
85 90 95

Tyr Cys Ala Arg Ala Arg Ala Ala Gly Thr Ile Phe Asp Tyr Trp Gly 100 105 110

Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile Gln Met Thr Gln 130 135 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr 145 150 155 160

Cys Arg Ala Ser Gln Asn Val Ser Asn Tyr Leu Thr Trp Tyr Gln Gln 165 170 175

Lys Pro Gly Lys Ala Gly Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu 180 185 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp 195 200 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr 215

Tyr Cys Gln Gln Ser Tyr Phe Asn Pro Ala Thr Phe Gly Gln Gly Thr 235

Lys Leu Glu Ile Lys Arg Ala Ala 245

<210> 11

<211> 769

<212> DNA

<213> Artificial sequence

<220>

<223> scFv SC02021

<220>

<221> CDS

<222> (3)..(767)

<223>

<400> 11 cc atg gct gag gtg cag ctg gtg gag tct ggg gga ggc ttg gta cag 47 Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln 10 cct agg ggg tcc ctg aga ctc tcc tgt gca gcc tct gga ttc acc ttt 95 Pro Arg Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe 20 25 age age tae geg atg aac tgg gte ege cag geg eee ggg aag ggg etg 143 Ser Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu gag tgg gtg gca gtt ata tca tat gat gga agc aat aaa tac tac gca 191 Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala 50 gac tcc gtg aag ggc cga ttc acc atc tcc aga gac aat tcc aag aac 239 Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn 65 70 acg ctg tat ctg caa atg aac agc ctg aga gct gag gac aca gcc gtg 287 Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val tat tac tgt gcc aaa gac cgc tac atc acg ttg ccg aac gcg ttg gat 335 Tyr Tyr Cys Ala Lys Asp Arg Tyr Ile Thr Leu Pro Asn Ala Leu Asp 105 tac tgg ggc cag ggc acc ctg gtg acc gtg ctc gag ggt acc gga ggt

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly 120

383

tcc Ser	ggc Gly	gga Gly 130	acc Thr	ggg Gly	tct Ser	Gly ggg	act Thr 135	ggt Gly	acg Thr	agc Ser	gag Glu	ctc Leu 140	gac Asp	atc Ile	cag Gln	431
atg Met	acc Thr 145	cag Gln	tct Ser	cca Pro	gtc Val	tca Ser 150	ctg Leu	ccc Pro	gtc Val	acc Thr	cct Pro 155	gga Gly	gag Glu	ccg Pro	gcc Ala	479
tcc Ser 160	atc Ile	tcc Ser	tgc Cys	agg Arg	tct Ser 165	agt Ser	cag Gln	agc Ser	ctc Leu	ctg Leu 170	cat His	agt Ser	aat Asn	gga Gly	tac Tyr 175	527
aac Asn	tat Tyr	ttg Leu	gat Asp	tgg Trp 180	tac Tyr	ctg Leu	cag Gln	aag Lys	cca Pro 185	GJ À aaa	cag Gln	tct Ser	cca Pro	cag Gln 190	ctc Leu	575
ctg Leu	atc Ile	tat Tyr	ttg Leu 195	ggt Gly	tct Ser	aat Asn	cgg Arg	gcc Ala 200	tcc Ser	GJ À GG À	gtc Val	cct Pro	gac Asp 205	agg Arg	ttc Phe	623
agt Ser	ggc Gly	agt Ser 210	gga Gly	tca Ser	ggc Gly	aca Thr	gat Asp 215	ttt Phe	aca Thr	ctg Leu	aaa Lys	atc Ile 220	agc Ser	aga Arg	gtg Val	671
gag Glu	gct Ala 225	gag Glu	gat Asp	gtt Val	GJA āāā	gtt Val 230	tat Tyr	tac Tyr	tgc C y a	cag Gln	cag Gln 235	tac Tyr	aag Lys	tcg Ser	aac Asn	719
ccg Pro 240	ccc Pro	acc Thr	ttc Phe	ggc Gly	cag Gln 245	ggc Gly	acc Thr	aaa Lys	gtg Val	gaa Glu 250	atc Ile	aaa Lys	cgc Arg	gcg Ala	gcc Ala 255	767
gc																769

<210> 12

<211> 255

<212> PRT

<213> Artificial sequence

<220>

<223> scFv SC02021

<400> 12

Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro 1 $$ 5 $$ 10 $$ 15

Arg Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser 20 25 30

Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu 35 40

Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp 50 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr 85 90 95

Tyr Cys Ala Lys Asp Arg Tyr Ile Thr Leu Pro Asn Ala Leu Asp Tyr 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser 115 120 125

Gly Gly Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile Gln Met 130 140

Thr Gln Ser Pro Val Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser 145 150 155 160

Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn 165 170 175

Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu 180 185 190

Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser 195 200 205

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu 210 215 220

Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr Lys Ser Asn Pro 225 230 235 240

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Ala Ala 245 250 255

<210> 13

<211> 745

<212> DNA

<213> Artificial sequence

<220>

<223> scfv SC02022

<220>

<221> CDS

<222> (3)..(743)

	atg	13 gcc Ala	gag Glu	gtg Val	cag Gln 5	ctg Leu	gtg Val	gag Glu	tct Ser	ggg Gly 10	gga Gly	Gly ggc	ttg Leu	Val	cat His 15	47
cct Pro	GJA aaa	ej aaa	tcc Ser	ctg Leu 20	aga Arg	ctc Leu	tcc Ser	tgt Cys	gca Ala 25	ggc	tct Ser	gga Gly	ttc Phe	acc Thr 30	ttc Phe	95
agt Ser	agc Ser	tat Tyr	gct Ala 35	atg Met	cac His	tgg Trp	gtt Val	cgc Arg 40	cag Gln	gct Ala	cca Pro	gga Gly	aaa Lys 45	ggt Gly	ctg Leu	143
gag Glu	tgg Trp	gta Val 50	tca Ser	gct Ala	att Ile	ggt Gly	acc Thr 55	ggt Gly	ggt Gly	ggc	aca Thr	tac Tyr 60	tat Tyr	gca Ala	gac Asp	191
tcc Ser	gtg Val 65	cag Gln	ggc Gly	cga Arg	ttc Phe	acc Thr 70	atc Ile	tcc Ser	aga Arg	gac Asp	aat Asn 75	gcc Ala	aag Lys	aac Asn	tcc Ser	239
ttg Leu 80	tat Tyr	ctt Leu	caa Gln	atg Met	aac Asn 85	agc Ser	ctg Leu	aga Arg	gcc Ala	gag Glu 90	gac Asp	acg Thr	gcc Ala	gtg Val	tat Tyr 95	287
tac Tyr	tgt Cys	gca Ala	aga Arg	tac Tyr 100	gac Asp	gag Glu	ccg Pro	ctg Leu	acg Thr 105	att Ile	tac Tyr	tgg Trp	ttt Phe	gac Asp 110	tcc Ser	335
tgg Trp	ggc Gly	caa Gln	ggt Gly 115	acc Thr	ctg Leu	gtc Val	acc Thr	gtc Val 120	tcg Ser	agt Ser	ggt Gly	gga Gly	ggc Gly 125	ggt Gly	tca Ser	383
ggc Gly	gga Gly	ggt Gly 130	ggc Gly	tct Ser	ggc Gly	ggt Gly	ggc Gly 135	gga Gly	tcg Ser	gaa Glu	att Ile	gag Glu 140	ctc Leu	aca Thr	cag Gln	431
Ser	Pro 145	Ala	Thr	Leu	tct Ser	Leu 150	Ser	Pro	Gly	Glu	Arg 155	Ala	Thr	Leu	Ser	479
Cys 160	Arg	Ala	Ser	Gln	agt Ser 165	Val	Ser	Ser	Tyr	Leu 170	Ala	Trp	Tyr	Gln	Gln 175	527
aaa Lys	cct Pro	ggc Gly	cag Gln	gct Ala 180	ccc Pro	agg Arg	ctc Leu	ctc Leu	atc Ile 185	tat Tyr	gat Asp	gca Ala	tcc Ser	aac Asn 190	agg Arg	575
gcc Ala	act Thr	ggc Gly	atc Ile 195	cca Pro	gcc Ala	agg Arg	ttc Phe	agt Ser 200	ggc Gly	agt Ser	Gly	tct Ser	ggg Gly 205	aca Thr	gac Asp	623
ttc Phe	act Thr	ctc Leu 210	acc Thr	atc Ile	agc Ser	agc Ser	cta Leu 215	gag Glu	cct Pro	gaa Glu	gat Asp	ttt Phe 220	gca Ala	gtt Val	tat Tyr	671
tac Tyr	tgt Cys 225	cag Gln	cag Gln	cgt Arg	agc Ser	aac Asn 230	tgg Trp	cct Pro	ccg Pro	gct Ala	ttc Phe 235	ggc Gly	gga Gly	ej aaa	acc Thr	719
aag Lys 240	gtg Val	gag Glu	atc Ile	aaa Lys	cgt Arg 245	gcg Ala	gcc Ala	gc								745

<210> 14

<211> 247

<212> PRT

<213> Artificial sequence

<220>

<223> scFv SC02022

<400> 14

Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val His Pro 1 5 10 15

Gly Gly Ser Leu Arg Leu Ser Cys Ala Gly Ser Gly Phe Thr Phe Ser 20 25 30

Ser Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu 35 40

Trp Val Ser Ala Ile Gly Thr Gly Gly Gly Thr Tyr Tyr Ala Asp Ser 50 55 60

Val Gln Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu 65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr 85 90 95

Cys Ala Arg Tyr Asp Glu Pro Leu Thr Ile Tyr Trp Phe Asp Ser Trp 100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly 115 120 125

Gly Gly Gly Ser Gly Gly Gly Ser Glu Ile Glu Leu Thr Gln Ser 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys 165 170 175

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala 180 185

Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe 195 200 205

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr 210 215

Cys Gln Gln Arg Ser Asn Trp Pro Pro Ala Phe Gly Gly Gly Thr Lys 230 235

Val Glu Ile Lys Arg Ala Ala 245

<210> 15

<211> 745

<212> DNA

<213> Artificial sequence

<220>

<223> scFv SC02023

<220>

<221> CDS

<222> (3)..(743)

<223>

cc atg gcc gag gtg cag ctg gtg gag tct ggg gga ggc ttg gta cat 47 Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val His 10

cet ggg ggg tee etg aga ete tee tgt gea gge tet gga tte ace tte 95 Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Gly Ser Gly Phe Thr Phe

agt agc tat gct atg cac tgg gtt cgc cag gct cca gga aaa ggt ctg 143 Ser Ser Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 35 4 N

gag tgg gta tca gct att ggt act ggt ggc aca tac tat gca gac 191 Glu Trp Val Ser Ala Ile Gly Thr Gly Gly Gly Thr Tyr Ala Asp 50

tcc gtg atg ggc cgg ttc acc atc tcc aga gac aat tcc aag aac acg 239 Ser Val Met Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr

ctg tat ctg caa atg aac agc ctg aga gcc gag gac acg gcc gtg tat 287 Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr 85

tac tgt gca aga tac gac aat gtg atg ggt ctt tac tgg ttt gac tac 335 Tyr Cys Ala Arg Tyr Asp Asn Val Met Gly Leu Tyr Trp Phe Asp Tyr 105

tgg ggc caa ggt acc ctg gtc acc gtc tcg agt ggt gga ggc ggt tca 383

WO 03/106498	PCT/EP03/06341
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Ser 115 120 125	
ggc gga ggt ggc tct ggc ggt ggc gga tcg gaa att gag ctc aca cag Gly Gly Gly Ser Gly Gly Gly Ser Glu Ile Glu Leu Thr Gln 130 135 140	431
tct cca gcc acc ctg tct ttg tct cca ggg gaa aga gcc acc ctc tcc Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser 145 150 155	479
tgc agg gcc agt cag agt gtt agc agc tac tta gcc tgg tac caa cag Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr Gln Gln 160 165 170 175	. 527
aaa cct ggc cag gct ccc agg ctc ctc atc tat gat gca tcc aac agg Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg 180 185 190	575
gcc act ggc atc cca gcc agg ttc agt ggc agt ggg tct ggg aca gac Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp 195 200 205	623
ttc act ctc acc atc agc agc cta gag cct gaa gat ttt gca gtt tat Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr 210 215 220	671
tac tgt cag cag cgt agc aac tgg cct ccg gct ttc ggc gga ggg acc Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro Ala Phe Gly Gly Gly Thr 225 230 235	719
aag gtg gag atc aaa cgt gcg gcc gc Lys Val Glu Ile Lys Arg Ala Ala 240 245	745
<210> 16	
<211> 247	
<212> PRT	
<213> Artificial sequence	
<220>	
<223> scFv SC02023	
<400> 16	
Met Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val His Pro 1 5 10 15	
Gly Gly Ser Leu Arg Leu Ser Cys Ala Gly Ser Gly Phe Thr Phe Ser 20 25 30	
Ser Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu 35 40 45	
Trp Val Ser Ala Ile Gly Thr Gly Gly Gly Thr Tyr Tyr Ala Asp Ser 50 60	

:,

Val Met Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu 65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr 85 90 95

Cys Ala Arg Tyr Asp Asn Val Met Gly Leu Tyr Trp Phe Asp Tyr Trp 100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly 115 120 125

Gly Gly Gly Ser Gly Gly Gly Ser Glu Ile Glu Leu Thr Gln Ser 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys 145 150 155 160

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys 165 170 175

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala 180 185 190

Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe 195 200 205

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr 210 215 220

Cys Gln Gln Arg Ser Asn Trp Pro Pro Ala Phe Gly Gly Gly Thr Lys 225 230 235 240

Val Glu Ile Lys Arg Ala Ala

<210> 17

<211> 12

<212> PRT

<213> Artificial sequence

<220>

<223> CDR3 of scFv SC02008

<400> 17

Asp Arg Tyr Ser Gln Val His Tyr Ala Leu Asp Tyr 1 5 10

2 0

<210> 18

<211> 12

<212> PRT

<213> Artificial sequence

<220>

<223> CDR3 of scFv SC02009

<400> 18

Asp Arg Tyr Val Asn Thr Ser Asn Ala Phe Asp Tyr 1 5 10

<210> 19

<211> 10

<212> PRT

<213> Artificial sequence

<220>

<223> CDR3 of scFv SC02010

<400> 19

Asp Met Ser Gly Phe His Glu Phe Asp Tyr 1 5 10

<210> 20

<211> 12

<212> PRT

<213> Artificial sequence

<220>

<223> CDR3 of scFv SC02011

<400> 20

Asp Arg Tyr Phe Arg Gln Gln Asn Ala Phe Asp Tyr 1 5

<210> 21

<211> 10

<212> PRT

<213> Artificial sequence

```
<220>
<223> CDR3 of scFv SC02012
<400> 21
Ala Arg Ala Ala Gly Thr Ile Phe Asp Tyr
<210> 22
<211> 12
<212> PRT
<213> Artificial sequence
<220>
<223> CDR3 of scFv SC02021
<400> 22
Asp Arg Tyr Ile Thr Leu Pro Asn Ala Leu Asp Tyr
1 5
<210> 23
<211> 12
<212> PRT
<213> Artificial sequence
<220>
<223> CDR3 of scFv SC02022
<400> 23
Tyr Asp Glu Pro Leu Thr Ile Tyr Trp Phe Asp Ser
              5
<210> 24
<211> 12
<212> PRT
<213> Artificial sequence
<220>
<223> CDR3 of scFv SC02023
<400> 24
```

Tyr Asp Asn Val Met Gly Leu Tyr Trp Phe Asp Tyr 1 5 10

<210> 25

<211> 451

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of heavy chain of 008

<400> 25

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr 20 25 30

Thr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asp Arg Tyr Ser Gln Val His Tyr Ala Leu Asp Tyr Trp Gly 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 145 150 155

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 . 250 . 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His 260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr 290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly 305 310 315

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser 355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435

Pro Gly Lys 450

25/46

<210> 26

<211> 449

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of heavy chain of 011

<400> 26

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr 20 25 30

Thr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40

Ser Ser Ile Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Arg Lys Gly 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln 65 70 75 80

Met Asn Asn Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg

Asp Arg Tyr Phe Arg Gln Gln Asn Ala Phe Asp Tyr Trp Gly Gln Gly 100 105 110

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe 115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu 130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp 145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu 165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser 180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro 195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys 210 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro 225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser 245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp 260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn 275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val 290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu 305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr 340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys $405 \hspace{1.5cm} 410 \hspace{1.5cm} 415 \hspace{1.5cm}$

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly 435 440

Lys

<210> 27

<211> 451

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of heavy chain 021

<400> 27

Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Arg Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val 50 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Lys Asp Arg Tyr Ile Thr Leu Pro Asn Ala Leu Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His 260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr 290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly 305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser 355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435 440 445

Pro Gly Lys 450

<210> 28

<211> 450

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of heavy chain of 023

<400> 28

Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val His Pro Gly Gly 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Gly Ser Gly Phe Thr Phe Ser Ser Tyr 20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ser Ala Ile Gly Thr Gly Gly Gly Thr Tyr Tyr Ala Asp Ser Val Met 50 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Arg Tyr Asp Asn Val Met Gly Leu Tyr Trp Phe Asp Tyr Trp Gly Gln 100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 . 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly 225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile 245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg 290 295 . 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys 305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu 325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr 340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu 355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val 385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp 405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His 420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro 435 440 445

Gly Lys 450

<210> 29

<211> 219

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of light chain of 008

<400> 29

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser 20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Ala Gly Gln Ser 35 40

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro 50 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr 85 90 95

Tyr Asn His Pro Thr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu 115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe 130 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln 145 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser 165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu 180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser 195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys 210 215

<210> 30

<211> 219

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of light chain of 011

<400> 30

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Pro Val Thr Pro Gly 1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser 20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Ala Gly Gln Ser 35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro 50 55

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr 85 90 95

Tyr Asn His Pro Thr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu 115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe 130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln 145 150 155

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser 165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu 180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser 195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys 210 215

<210> 31

<211> 219

2 0

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of light chain of 021

<400> 31

Asp Ile Gln Met Thr Gln Ser Pro Val Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser 20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser 35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro 50 55

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr 85 90 95

Lys Ser Asn Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys 100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu 115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe 130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln 145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser 165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser 195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys 210 215

<210> 32

<211> 214

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of light chain of 023

<400> 32

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile 35 40

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro 65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro 85 90

Ala Phe Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala 100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205

```
Phe Asn Arg Gly Glu Cys
   210
<210> 33
<211> 55
<212> DNA
<213> Artificial sequence
<220>
<223> 5' cloning site of pPicZalphaB
<220>
<221> CDS
<222> (1)..(54)
<223>
<400> 33
tct ctc gag aaa aga gag gct gaa gct gca gga att cac gtg gcc cag
                                                                    48
Ser Leu Glu Lys Arg Glu Ala Glu Ala Gly Ile His Val Ala Gln
ccg gcc g
                                                                    55
Pro Ala
<210> 34
<211> 18
<212> PRT
<213> Artificial sequence
<220>
<223> 5' cloning site of pPicZalphaB
<400> 34
Ser Leu Glu Lys Arg Glu Ala Glu Ala Gly Ile His Val Ala Gln
Pro Ala
<210> 35
<211> 55
<212> DNA
```

```
<213> Artificial sequence
<220>
<223> 5' cloning site of pPicZFVH
<220>
<221> CDS
<222> (1)..(54)
<223>
<400> 35
tct ctc gag aaa aga gcc atg gaa gct gca gga att cac gtg gcc cag
Ser Leu Glu Lys Arg Ala Met Glu Ala Ala Gly Ile His Val Ala Gln
                                                                              48
ccg gcc g
                                                                              55
Pro Ala
<210> 36
<211> 18
<212> PRT
<213> Artificial sequence
<220>
<223> 5' cloning site of pPicZFVH
<400> 36
Ser Leu Glu Lys Arg Ala Met Glu Ala Ala Gly Ile His Val Ala Gln
                 5
Pro Ala
<210> 37
<211> 92
<212> DNA
<213> Artificial sequence
<220>
<223> Synthetic hinge region
```

37/46

<220>

<221> CDS

<222> (1)..(90)

<223>

<400> 37

gcg gcc gcg cca aag cca agt acc cca cca ggt tct tca tgt cca cca 48
Ala Ala Pro Lys Pro Ser Thr Pro Pro Gly Ser Ser Cys Pro Pro
1 5 10 15

tgt cca ggc tct ggc ggt gcg cca atc gat agc ggc ttt cta ga 92 Cys Pro Gly Ser Gly Gly Ala Pro Ile Asp Ser Gly Phe Leu 20 25 30

<210> 38

<211> 30

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic hinge region

<400> 38

Cys Pro Gly Ser Gly Gly Ala Pro Ile Asp Ser Gly Phe Leu 20 25 30

<210> 39

<211> 1416

<212> DNA

<213> Artificial sequence

<220>

<223> Nucleotide sequence of heavy chain of 008

<400> 39

atggcatgcc ctggcttcct gtgggcactt gtgatctcca cctgtcttga attctccatg

gccgaggtgc agctggtgga gtctggggga ggcttggtcc agcctggagg gtccctgaga

120

ctctcctgtg cagcctctgg attcaccttt agcaactaca cgatgaactg ggtccgccag

180

gcgcccggga aggggctgga gtgggtctca gctattagtg gtagtggtgg tagcacatac

240

tacgcagact ccgtgaaggg ccggttcacc atctccagag acaattccaa gaacacgctg

300

tatctgcaaa tgaacagcct gagagccgag gacacggccg tgtattactg tgccaaagac

360

cgctactccc	aggtgcacta	cgcgttggat	tactggggcc	agggcaccct	ggtgaccgtc	420
tcctcagcct	ccaccaaggg	cccatcggtc	ttccccctgg	caccctcctc	caagagcacc	480
tctgggggca	cagcggccct	gggctgcctg	gtcaaggact	acttccccga	accggtgacg	540
gtgtcgtgga	actcaggcgc	cctgaccagc	ggcgtgcaca	ccttcccggc	tgtcctacag	600
tcctcaggac	tctactccct	cagcagcgtg	gtgaccgtgc	cctccagcag	cttgggcacc	660
cagacctaca	tctgcaacgt	gaatcacaag	cccagcaaca	ccaaggtgga	caagagagtt	720
gagcccaaat	cttgtgacaa	aactcacaca	tgcccaccgt	gcccagcacc	tgaactcctg	780
gggggaccgt	cagtcttcct	cttcccccca	aaacccaagg	acaccctcat	gatctcccgg	840
acccctgagg	tcacatgcgt	ggtggtggac	gtgagccacg	aagaccctga	ggtcaagttc	900
aactggtacg	tggacggcgt	ggaggtgcat	aatgccaaga	caaagccgcg	ggaggagcag	960
tacaacagca	cgtaccgtgt	ggtcagcgtc	ctcaccgtcc	tgcaccagga	ctggctgaat	1020
ggcaaggagt	acaagtgcaa	ggtctccaac	aaagccctcc	cagcccccat	cgagaaaacc	1080
atctccaaag	ccaaagggca	gccccgagaa	ccacaggtgt	acaccctgcc	cccatcccgg	1140
gaggagatga	ccaagaacca	ggtcagcctg	acctgcctgg	tcaaaggctt	ctatcccagc	1200
gacategeeg	tggagtggga	gagcaatggg	cagccggaga	acaactacaa	gaccacgcct	1260
cccgtgctgg	actccgacgg	ctccttcttc	ctctatagca	agctcaccgt	ggacaagagc	1320
aggtggcagc	aggggaacgt	cttctcatgc	tccgtgatgc	atgaggctct	gcacaaccac	1380
tacacgcaga	agagcctctc	cctgtctccg	ggtaaa			1416

<210> 40

<211> 1410

<212> DNA

<213> Artificial sequence

<220>

<223> Nucleotide sequence of heavy chain of 011

<400> 40 atggcatgcc ctggcttcct gtgggcactt gtgatctcca cctgtcttga attctccatg 60 gccgaggtgc agctggtgga gtctggggga ggcgtggtcc agcctgggag gtccctgaga 120 ctctcctgtg cagcctctgg attcaccttc agcgactaca cgatgaactg ggtccgccag 180 gcgcccggga aggggctgga gtgggtctca tccattagtg gtggtagcac atactacgca 240 gactccagga agggcagatt caccatctcc agagacaatt ccaagaacac gctgtatctt 300 caaatgaaca acctgagagc tgaggacacg gccgtgtatt actgtgcaag agaccgctac 360 ttcaggcagc agaacgcgtt cgattactgg ggccagggca ccctggtgac cgtctcctca 420 gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 480

2 4

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 540 tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 600 ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 660 tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagag agttgagccc 720 aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 780 ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 840 gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 900 tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacaac 960 agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 1020 gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 1080 aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 1140 atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 1200 gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 1260 ctggactccg acggctcctt cttcctctat agcaagctca ccgtggacaa gagcaggtgg 1320 cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 1380 cagaagagcc tctccctgtc tccgggtaaa 1410

<210> 41

<211> 1416

WO 03/106498

<212> DNA

<213> Artificial sequence

<220>

<223> Nucleotide sequence of heavy chain of 021

atggcatgcc ctggcttcct gtgggcactt gtgatctcca cctgtcttga attctccatg 60 gccgaggtgc agctggtgga gtctggggga ggcttggtac agcctagggg gtccctgaga 120 ctctcctgtg cagcctctgg attcaccttt agcagctacg cgatgaactg ggtccgccag 180 gcgcccggga aggggctgga gtgggtggca gttatatcat atgatggaag caataaatac 240 tacgcagact ccgtgaaggg ccgattcacc atctccagag acaattccaa gaacacgctg 300 tatctgcaaa tgaacagcct gagagctgag gacacagccg tgtattactg tgccaaagac 360 cgctacatca cgttgccgaa cgcgttggat tactggggcc agggcaccct ggtgaccgtc 420 tecteageet ceaceaaggg eccateggte tteceetgg eaceeteete caagageace 480 tctgggggca cagcggccct gggctgcctg gtcaaggact acttccccga accggtgacg 540 gtgtcgtgga actcaggcgc cctgaccagc ggcgtgcaca ccttcccggc tgtcctacag 600

tcctcaggac	tctactccct	cagcagcgtg	gtgaccgtgc	cctccagcag	cttgggcacc	660
cagacctaca	tctgcaacgt	gaatcacaag	cccagcaaca	ccaaggtgga	caagagagtt	720
gagcccaaat	cttgtgacaa	aactcacaca	tgcccaccgt	gcccagcacc	tgaactcctg	780
gggggaccgt	cagtcttcct	cttcccccca	aaacccaagg	acaccctcat	gatctcccgg	840
acccctgagg	tcacatgcgt	ggtggtggac	gtgagccacg	aagaccctga	ggtcaagttc	900
aactggtacg	tggacggcgt	ggaggtgcat	aatgccaaga	caaagccgcg	ggaggagcag	960
tacaacagca	cgtaccgtgt	ggtcagcgtc	ctcaccgtcc	tgcaccagga	ctggctgaat	1020
ggcaaggagt	acaagtgcaa	ggtctccaac	aaagccctcc	cagcccccat	cgagaaaacc	1080
atctccaaag	ccaaagggca	gccccgagaa	ccacaggtgt	acaccctgcc	cccatcccgg	1140
gaggagatga	ccaagaacca	ggtcagcctg	acctgcctgg	tcaaaggctt	ctatcccagc	1200
gacatcgccg	tggagtggga	gagcaatggg	cagccggaga	acaactacaa	gaccacgcct	1260
cccgtgctgg	actccgacgg	ctccttcttc	ctctatagca	agctcaccgt	ggacaagagc	1320
aggtggcagc	aggggaacgt	cttctcatgc	tccgtgatgc	atgaggctct	gcacaaccac	1380
tacacgcaga	agagcctctc	cctgtctccg	ggtaaa			1416

<210> 42

<211> 1413

<212> DNA

<213> Artificial sequence

ĩ

<220>

<223> Nucleotide sequence of heavy chain of 023

atggcatgcc ctggcttcct gtgggcactt gtgatctcca cctgtcttga attctccatg 60 gccgaggtgc agctggtgga gtctggggga ggcttggtac atcctggggg gtccctgaga 120 ctctcctgtg caggctctgg attcaccttc agtagctatg ctatgcactg ggttcgccag 180 gctccaggaa aaggtctgga gtgggtatca gctattggta ctggtggtgg cacatactat 240 gcagactccg tgatgggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 300 ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc aagatacgac 360 aatgtgatgg gtctttactg gtttgactac tggggccagg gcaccctggt gaccgtctcc 420 tcagcctcca ccaagggccc atcggtcttc ccctggcac cctcctccaa gagcacctct 480 gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 540 tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 600 . tcaggactet actecetcag cagegtggtg accgtgeect ccageagett gggeacceag 660 acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gagagttgag 720

cccaaatctt	gtgacaaaac	tcacacatgc	ccaccgtgcc	cagcacctga	actcctgggg	780
ggaccgtcag	tcttcctctt	cccccaaaa	cccaaggaca	ccctcatgat	ctcccggacc	840
cctgaggtca	catgcgtggt	ggtggacgtg	agccacgaag	accctgaggt	caagttcaac	900
tggtacgtgg	acggcgtgga	ggtgcataat	gccaagacaa	agccgcggga	ggagcagtac	960
aacagcacgt	accgtgtggt	cagcgtcctc	accgtcctgc	accaggactg	gctgaatggc	1020
aaggagtaca	agtgcaaggt	ctccaacaaa	gccctcccag	cccccatcga	gaaaaccatc	1080
tccaaagcca	aagggcagcc	ccgagaacca	caggtgtaca	ccctgccccc	atcccgggag	1140
gagatgacca	agaaccaggt	cagcctgacc	tgcctggtca	aaggcttcta	tcccagcgac	1200
atcgccgtgg	agtgggagag	caatgggcag	ccggagaaca	actacaagac	cacgcctccc	1260
gtgctggact	ccgacggctc	cttcttcctc	tatagcaagc	tcaccgtgga	caagagcagg	1320
tggcagcagg	ggäacgtctt	ctcatgctcc	gtgatgcatg	aggctctgca	caaccactac	1380
acgcagaaga	gcctctccct	gtctccgggt	aaa			1413

<210> 43

<211> 720

<212> DNA

<213> Artificial sequence

<220>

<223> Nucleotide sequence of light chain of 008

<400> 43 atggcatgcc ctggcttcct gtgggcactt gtgatctcca cctgtctcga gttttccatg 60 gctgacatcg tgatgacaca gtctccagac tcactgcccg tcacccctgg agagccggcc 120 tccatctcct gcaggtctag tcagagcctc ctgcatagta atggatacaa ctatttggat 180 tggtacctgc agaaggcagg gcagtctcca cagctcctga tctatttggg ttctaatcgg 240 gcctccgggg tccctgacag gttcagtggc agtggatcag gcacagattt tacactgaaa 300 360 atcagcagag tggaggctga ggatgttggg gtttattact gccagcagta ctacaaccac ccgacgacct tcggccaggg caccaaactg gaaatcaaac gtactgtggc tgcaccatct 420 gtcttcatct tcccgccatc tgatgagcag ttgaaatctg gaactgcctc tgttgtgtgc 480 ctgctgaata acttctatcc cagagaggcc aaagtacagt ggaaggtgga taacgccctc 540 600 caatcgggta actcccagga gagtgtcaca gagcaggaca gcaaggacag cacctacagc 660 ctcagcagca ccctgacgct gagcaaagca gactacgaga aacacaaagt ctacgcctgc gaagtcaccc atcagggcct gagctcgccc gtcacaaaga gcttcaacag gggagagtgt 720

<210> 44

<211> 720

<212> DNA

<213> Artificial sequence

<220>

<223> Nucleotide sequence of light chain of 011

<400> atggcatgcc ctggcttcct gtgggcactt gtgatctcca cctgtctcga gttttccatg 60 gctgacatcg tgatgacaca gtctccagtc accctgcccg tcacccctgg agagccggcc 120 tccatctcct gcaggtctag tcagagcctc ctgcatagta atggatacaa ctatttggat 180 240 tggtacctgc agaagccagg gcagtctcca cagctcctga tctatttggg ttctaatcgg 300 gcctccgggg tccctgacag gttcagtggc agtggatcag gcacagattt tacactgaaa atcagcagag tggaggctga ggatgttggg gtttattact gccagcagta cctcacggcc 360 420 ccgccacct tcggccaggg caccaaactg gaaatcaaac gtactgtggc tgcaccatct 480 gtcttcatct tcccgccatc tgatgagcag ttgaaatctg gaactgcctc tgttgtgtgc ctgctgaata acttctatcc cagagaggcc aaagtacagt ggaaggtgga taacgccctc 540 600 caatcgggta actcccagga gagtgtcaca gagcaggaca gcaaggacag cacctacagc 660 ctcagcagca ccctgacgct gagcaaagca gactacgaga aacacaaagt ctacgcctgc gaagtcaccc atcagggcct gagctcgccc gtcacaaaga gcttcaacag gggagagtgt 720

<210> 45

<211> 720

<212> DNA

<213> Artificial sequence

<220>

<223> Nucleotide sequence of light chain of 021

60 atggcatgcc ctggcttcct gtgggcactt gtgatctcca cctgtctcga gttttccatg gctgacatcc agatgaccca gtctccagtc tcactgcccg tcacccctgg agagccggcc 120 tccatctcct gcaggtctag tcagagcctc ctgcatagta atggatacaa ctatttggat 180 tggtacctgc agaagccagg gcagtctcca cagctcctga tctatttggg ttctaatcgg 240 qcctccgggg tccctgacag gttcagtggc agtggatcag gcacagattt tacactgaaa 300 360 atcagcagag tggaggctga ggatgttggg gtttattact gccagcagta caagtcgaac 420 ccgcccacct tcggccaggg caccaaagtg gaaatcaaac gtactgtggc tgcaccatct 480 qtcttcatct tcccgccatc tgatgagcag ttgaaatctg gaactgcctc tgttgtgtgc

Ξ.

540 ctgctgaata acttctatcc cagagaggcc aaagtacagt ggaaggtgga taacgccctc 600 caatcgggta actcccagga gagtgtcaca gagcaggaca gcaaggacag cacctacagc 660 ctcagcagca ccctgacgct gagcaaagca gactacgaga aacacaaagt ctacgcctgc 720 gaagtcaccc atcagggcct gagctcgccc gtcacaaaga gcttcaacag gggagagtgt <210> 46 <211> 705 <212> DNA <213> Artificial sequence <220> <223> Nucleotide sequence of light chain of 023 <400> 46 atggcatgcc ctggcttcct gtgggcactt gtgatctcca cctgtctcga gttttccatg 60 gctgaaattg tgctcacaca gtctccagcc accctgtctt tgtctccagg ggaaagagcc 120 180 accetetect geagggeeag teagagtgtt ageagetact tageetggta ceaacagaaa cetggceagg eteccagget ceteatetat gatgeateca acagggeeae tggcatecea 240 gccaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagcctagag 300 360 cctgaagatt ttgcagttta ttactgtcag cagcgtagca actggcctcc ggctttcggc 420 ggagggacca aggtggagat caaacgtact gtggctgcac catctgtctt catcttcccg ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc 480 tatcccagag aggccaaagt acagtggaag gtggataacg ccctccaatc gggtaactcc 540 caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcaccctg 600 660 acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt cacccatcag 705 qqcctqaqct cgcccgtcac aaagagcttc aacaggggag agtgt <210> 47 <211> 46 <212> DNA <213> Artificial sequence <220> <223> Primer

46

acctgtcttg aattctccat ggccgaggtg cagctggtgg agtctg

<400> 47

WO 03/106498		PCT/EP03/06341
<210> 48		
<211> 51		
<212> DNA		
<213> Artificial sequence		
<220>		
<223> Primer		
<400> 48 gctcgcggat ccactcacct gaggagacgg tcac	ccagggt gccctggccc c	51
<210> 49		
<211> 49		
<212> DNA		
<213> Artificial sequence		
<220>		
<223> Primer		
<400> 49 acctgtctcg agttttccat ggctgacatc gtg	atgacac agtctccag	49
<210> 50		
<211> 47		
<212> DNA		
<213> Artificial sequence		
<220>		
<223> Primer		
<400> 50 acctgtctcg agttttccat ggctgacatc gtg	gatgaccc agtetec	47
<210> 51		
<211> 54		
<212> DNA		
<213> Artificial sequence		
<220>		
<223> Primer		

WO 03/106498	PCT/EP03/06341
<400> 51 acctgtctcg agttttccat ggctgaaatt gtgctcacac agtctccagc cacc	54
<210> 52	
<211> 55	
<212> DNA	
<213> Artificial sequence	
<220>	
<223> Primer	
<400> 52 ttttccttag cggccgcaaa gtgcacttac gtttgatttc cagtttggtg ccctg	55
<210> 53	
<211> 55	
<212> DNA	
<213> Artificial sequence	
<220>	
<223> Primer	
<400> 53 ttttccttag cggccgcaaa gtgcacttac gtttgatttc cactttggtg ccctg	55
<210> 54	
<211> 55	
<212> DNA	
<213> Artificial sequence	
<220>	
<223> Primer	
<400> 54	55
tttteettag eggeegeaaa gtgeacttae gtttgatete eacettggte eetee	Jö

2 0